Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #54

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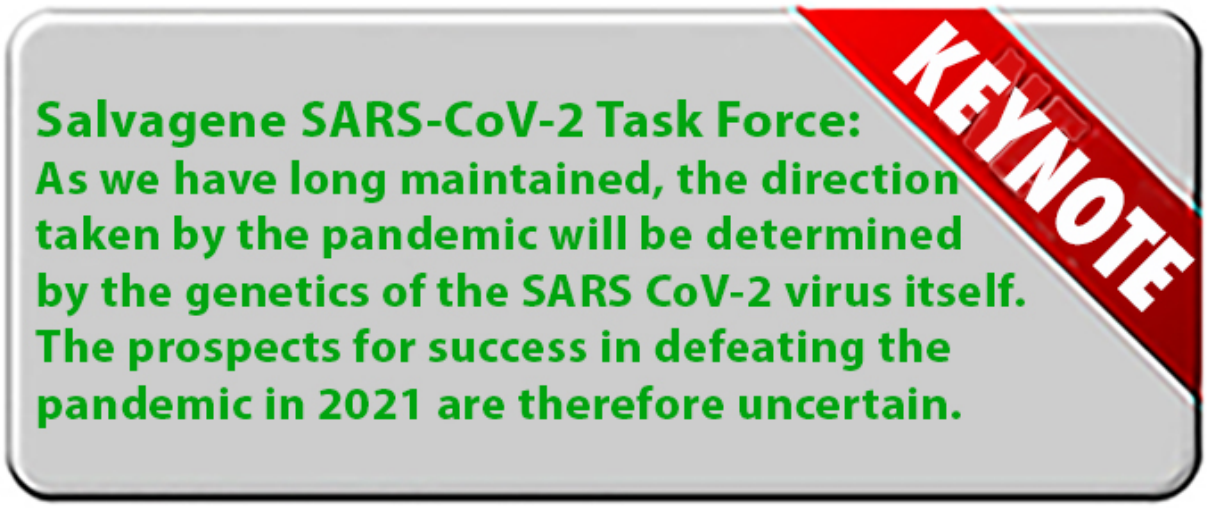

Dear Premium Customers,

SARS CoV-2 Task Force: As we have long maintained, the direction taken by the pandemic will be determined by the genetics of the SARS CoV-2 virus itself. The prospects for success in defeating the pandemic in 2021 are therefore uncertain.

As we flagged up in a previous Keynote, BioNTech and Pfizer have now officially confirmed that their vaccine retains its efficacy for both the B.1.1.7. and the 501Y.V2 variants. The 16 different mutations found in these two variants were tested and the manufacturer found that they made "no significant difference". The research has not yet been published, but we have been given a preview and our interpretation is that the BioNTech vaccine retains efficacy but it has not been proven that it can be maintained at the same rate as before.

Another caveat is that, while this assurance applies to mutations detected so far, no conclusions can be drawn about any future mutations further down the road. BioNTech/Pfizer were assisted in their research by the Department of Medicine at the University of Texas.

As we have stated on previous occasions, we have to consider the possibility that mutations will subsequently arise leading to variants that reduce vaccine efficacy. Salvagene's core expertise is in genetics, so we continue to maintain a keen and direct focus on further developments in the mutation of the SARS CoV-2 virus around the world.

For the time being, we are making our recommendations on vaccination only to Salvagene Premium clients who have highly elevated risk factors, i.e. Covid-19 Risk Factors higher than 1.5 paired with Cytokine Storm Risk Factors higher than 1.6. We recommend vaccination with the BioNTech/Pfizer products to risk-category clients as follows: with immediate effect in the UK, from 15th January in the USA, and from 20th January in the European Union. This is based on the availability of the production doses containing the new vaccine version in the respective countries.

We still do not recommend vaccination with Moderna and AstraZeneca to this high-risk group for the following reasons:
- Firstly, there is no reliable statement from the producers on the impact of the B.1.1.7. and 501Y.V2 variants;
- Secondly, we advise against using doses from the first production phase. The batches from the second production phase will reach the distributors towards the end of February at the earliest.

Unlike some specialists, we do not recommend making the interval between vaccinations more flexible, i.e. clients should only submit to the first dose if it is guaranteed that the second can be carried out three weeks later. We maintain that there are no reliable

studies as to the effect of a delayed second vaccination in the clinical phase, nor is it currently demonstrable.

As regards the AstraZeneca vaccine, the manufacturer has stated that the delayed booster (i.e. second jab) results in increased antibody retention. But the general problem here is that the delay of the second vaccination could lead to the coronavirus becoming resistant. Because of this theoretical possibility, we at Salvagene would not recommend it. The booster vaccination is essential. First and foremost, it is a matter of the T-memory cells which we have talked about on numerous occasions. Even before vaccine rollout began, we were already training and optimizing them in the course of our C-19 Immunization Program. The T-memory cells are the basis for immune memory – they build up protection in the long term. This is why the body's defenses have to be challenged more than once, thereby imprinting the cells so strongly that they can safely recognize and quickly neutralize the virus in the event of an infection.

We also currently advise against mixing the different vaccines. In theory, this could have a positive effect, but it is still too early to make any such recommendation. For foreign travel purposes, vaccines are mixed all the time. We know this from the clinical trials with Ebola.

Because we are familiar with all of the Covid-19 vaccine projects, we think it might be an option to have an mRNA vaccine as the first dose and a vector-based as the second. It is then possible that the immune response might be even stronger. However, this is something to be considered further down the line. We think it would only make sense if the mutation frequency and the severity of the mutations continue to increase, which we have to assume will happen. Other experts say that coronaviruses are relatively harmless and mutate at a slow rate. However, this has already been disproved with the currently known variants, with corresponding fatal consequences. We think that the most likely scenario is that the pandemic may develop in a similar seasonal

cycle over the long-term horizon, similar to influenza, and in this respect, vaccination strategies may develop further in the medium term and be complementary.

On the subject of gene mutation, we assume that it will be the decisive factor as far as the pandemic is concerned, both for the way in which the pandemic develops over the next few months and for the impact it will have on vaccination processes. That is why we have intensified our links with the gene sequencing centers in Tel Aviv and Cambridge (UK), in particular, the Wellcome Sanger Institute in Cambridge where truckloads of samples from the national testing laboratories across the UK arrive on a daily basis for sequencing. The work they do is of immense value to us as genetics specialists. A special department was set up ten months ago specifically to research coronavirus. Here we can see that B.1.1.7. is already found in 25 countries. The UK is a world leader in gene sequencing. It is also where the B.1.1.7. variant probably originated – a direct connection that we already reported on a week or so ago.

We take the B.1.1.7. variant (and also the 501Y.V2 variant) very seriously. Three percent of Londoners have already been infected with this variant, with correspondingly dire consequences. We do not agree with commentators who play down the significance of the B.1.1.7. variant, and we expect that it will spread very quickly to other countries. More than 170,000 genomes have so far been analyzed in the UK. The volume of data is almost overwhelming, and clearly variant B.1.1.7. is exactly the worst-case scenario we have been expecting for the past few months.

What is statistically interesting is that, while the overall case numbers halved in most UK regions during the November lock-down, they did not decrease in the south of England, the part of the country where the B.1.1.7. variant was strongly prevalent. From the evidence of throat swabs, we estimate that viral load is 10 times higher than with the old variant. The consequences are very clear in the UK at the moment. At the beginning of December,

0.3% of people in London were acutely ill with this variant; four weeks later it is already 3% of the total population – a tenfold increase. Only 0.5% of those infected in London succumbed to the old form of the virus, and this statistic has remained almost constant.

There are already 30% more patients in London's hospitals than at the height of the pandemic last April, which has prompted the Mayor of London to declare a "major incident". The average rate of new infections per 100,000 population is well over 1,000 across London, rising to nearly 1,600 per 100,000 in almost 60% of local health authorities. There are currently 7,000 people seriously ill with Covid-19 in hospitals, which inevitably means that the overall mortality rate is much higher, already standing at 50% more than last spring.

We will therefore continue to closely monitor both the mutation of the virus and the further development of the vaccines. We are confident that another mRNA-based candidate – this time from Curevac and our absolute top favorite – will be ready for rollout quite soon. In order to move the whole process along faster, Curevac has now also entered into a partnership agreement with pharmaceuticals giant Bayer.

We strongly recommend the PCR tests currently being used in the UK. B.1.1.7. happens to have a mutation in the spike protein that produces a characteristic pattern in the PCR tests commonly used in the UK. Thus, there is no need for costly additional tests to detect B.1.1.7. Clouding the prospects for success in combating the pandemic in 2021 is the likelihood that B.1.1.7. will spread further. This will make it much more difficult to achieve herd immunity, because the variant has a much higher R-value. Whereas we previously considered a herd immunity of 60% achieved by vaccination to be adequate, we now see the need for between 75-80%. Significantly more people will have to be vaccinated to bring the pandemic to an end.

We will continue to make individual recommendations on vaccination in the coming weeks. These will be guided by the availability of vaccines and the type of vaccine, as well as the individual health status of our clients.

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